REMARKS

This responds to the Office Action mailed on May 31, 2007.

Claim 107 has been added and claim 80 is canceled. As a result, claims 59-78 and 81-106 are now pending in this application. However, claims 59-73, 77, 85-106 are withdrawn from consideration. Accordingly, claims 74-76, 78, 81-84 and 107 are now under examination.

New claim 107 depends from claim 74 and states that the biosensor further comprises platelet derived growth factor (PDGF). Support for this subject matter can be found throughout the specification as originally filed, for example, in Example III which discloses that PDGF optimizes the chronotropic kinetics of stem cell-derived myocytes implanted at sites distant from the heart (see, e.g., page 25, line 28 to page 26, line 32).

The dependencies of claims 81-82 have also been amended and the term "mammal" has been changed to "mammalian subject."

Applicant submits that these changes do not constitute new matter.

§112 Rejection of the Claims

Claims 80-82 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner states that claims 80-82 depend from a cancelled claim. Claim 80 has been cancelled and claims 81-82 have been amended to depend from claim 74. In addition, the term "mammalian subject" is now used in claims 81-82 instead of "mammal." Applicant submits that claims 81-82 are definite and requests withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

§102 Rejection of the Claims

The Examiner has made two rejections of the present claims under section 102, which are addressed separately below.

A claim is anticipated under section 102 only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989).

To constitute anticipation, the claimed subject matter must be identically disclosed in the prior art. *In re Arkley*, 172 U.S.P.Q. 524 at 526 (C.C.P.A. 1972). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 101 (Fed. Cir. 1991). To overcome the defense of anticipation, "it is only necessary for the patentee to show some tangible difference between the invention and the prior art." *Del Mar Engineering Lab v. Physio-Tronics, Inc.*, 642 F.2d 1167, 1172, (9th Cir. 1981).

Moreover, an anticipation rejection that is based on inherency must be supported by factual and technical grounds establishing that the inherent feature must flow as a necessary conclusion, not simply a possible conclusion, from the teaching of the cited art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Int. 1990); *In re Oelrich*, 666 F.2d 578, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

U.S. Patent No. 5,368,028 to Palti (hereinafter "Palti")

Claims 74, 76-78 and 80-83 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,368,028 to Palti. According to the Examiner, Palti teaches the claimed invention, citing to Palti at col. 9, lines 16-31; at col. 6, lines 14-19; col. 11, lines 4-25; at col. 6, line 66 to col. 7, line 9; at col. 11, line 44 to col. 12, line 26.

Claim 74 is directed to an implantable physiological or pathophysiological biosensor comprising: in vitro or ex vivo modified stem cells coupled to an electrical interface and adapted to be electrically coupled to endogenous tissue or cells when implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject, wherein the in vitro or ex vivo modified stem cells can monitor a chemical, physiological or pathophysiological variable associated with the physiological or pathophysiological function of the subject and can produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.

Applicant submits that Palti is limited to implantable cells that may sense a chemical constituent in the blood. However, Palti fails to disclose at least the following elements:

(1) biosensors containing stem cells

(2) in vitro or ex vivo modified cells

(3) implantation of cells at a site distant from a natural site for a physiological or pathophysiological function

(4) production of a coagulation factor

(5) production of serotonin

(6) production of a growth factor

(7) production of a receptor

Instead of disclosing these elements, the focus of the Palti reference is on monitoring levels of chemicals in the blood using conventional cells and then separately administering a drug to correct those levels. The conventional cells that Palti uses are "chemosensitive" cells. However, these "chemosensitive" cells are just normal mammalian cells such as beta cells from the islets of Langerhans (see, e.g., Palti at col. 9, lines 25-51) and are not modified in vitro or ex vivo in any way. Hence, Palti fails to disclose at least one element of the claimed invention relating to in vitro or ex vivo modified cells. Such failure is significant because use of modified cells permits the skilled artisan to specifically design cell types that can not only detect changes in levels of blood chemicals but also directly treat problems that may arise by aberrant levels of blood chemicals.

The failure to disclose use of in vitro or ex vivo modified cells is illustrated by the failure of Palti to consider a more direct way to treat problems detected in chemical blood concentrations. For example, rather than disclosing that the "chemosensitive" cells produce agents that correct detected problems in chemical blood levels, Palti specifically discloses administration of drugs to correct any such aberrant levels of chemicals and does not disclose or contemplate use of the implanted cells themselves to correct these levels. For example, at col. 8, lines 2-4, Palti teaches that agents can be administered manually or by operation of an external or implanted pump. Thus, Palti does not contemplate or disclose use of in vitro or ex vivo modified cells that, for example, can produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.

As further evidence that Palti fails to disclose the present invention, Palti fails to disclose the following words that relate to the present claims:

- stem cells
- in vitro and ex vivo

- modify and modified
- recombinant
- genetic and genetically modified
- coagulation factor
- serotonin
- growth factor
- receptor

Applicant submits that Palti fails to disclose every element of the claimed invention and respectfully requests withdrawal of this rejection of claims 74, 76-78 and 80-83 under 35 U.S.C. § 102(b).

U.S. Patent Application Publication No. 2003/0211088 to Field (hereinafter "Field")

Claims 74-76 and 80-84 were rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent Application Publication No. 2003/0211088 to Field. According to the Examiner, Field discloses the invention (citing to Figure 1 and paragraphs 13, 18, 23-25, 40-42 and 62).

Claim 74 is directed to an implantable physiological or pathophysiological biosensor comprising: in vitro or ex vivo modified stem cells coupled to an electrical interface and adapted to be electrically coupled to endogenous tissue or cells when implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject, wherein the in vitro or ex vivo modified stem cells can monitor a chemical, physiological or pathophysiological variable associated with the physiological or pathophysiological function of the subject and can produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.

Applicant submits that Field fails to disclose at least the element relating to implantation into a mammalian subject at *a site distant* from a natural site for a physiological or pathophysiological function

Instead of disclosing implantation of biosensor cells at a site distant from a natural site for a physiological or pathophysiological function, Field is limited to disclosure of cardiomyocytes for graft implantation into the site where they are needed -- the heart. For

example, Field's Abstract provides evidence that Field does not disclose implantation at distal sites, as follows:

> Described are conduction cardiomyocyte-enriched cellular populations, and methods and materials for obtaining the same. The populations may be used to engraft mammalian myocardial tissue, for example to provide biological pacemakers. Also described are restorative cellular myocardial tissue, for example to provide biological pacemakers. Also described are restorative cellular myocardial grafts for improving the contractile function of injured segments of myocardium, and articles adapted for heart implantation (e.g. conductive pacemaker leads), which includes coatings of viable cardiomyocytes and optionally a carrier for the cardiomyocytes.

Thus, in one short paragraph, Field uses the phrases "used to engraft mammalian myocardial tissue," "myocardial grafts," "articles adapted for heart implantation" to indicate that the Field cells are implanted at the site where they are needed and are *not* implanted into a mammalian subject at a site *distant* from a natural site for a physiological or pathophysiological function. Accordingly, Field fails to disclose every element of the claimed invention.

The Examiner asserts that implantation into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function is merely an intended use having no patentable weight. However, the fact that the present biosensors are capable of detecting a physiological or pathophysiological function at sites distant from the natural site for that physiological or pathophysiological function means that the cells of the present invention have properties that Field's cells do not necessarily have.

In particular, the present application provides data demonstrating that cells such as cardiac myocytes sense and synchronize their chronotropic activity with endogenous tissues (e.g., the heart), even though the cells are not in direct contact with the heart (see Examples). Thus, the specification discloses how to make and use cells with optimal the chronotropic activity that also optimally synchronize their chronotropic biosensing activity with endogenous tissues (see Examples, including Example III). Nowhere does Field disclose any such cells that *from a distance* can detect and monitor such physiological activities.

Instead, Field requires use of "conduction cardiomycyes" and implantation into the site of physiological activity (i.e., in Field's case, the heart). Thus, Field requires that the cells "establish depolarization waves in the heart."

> In this regard, the fetal conduction cardiomyocytes utilized in the present invention will have the electrophysiologic properties consistent with pacemaker cells which act to establish depolarization waves in the heart.

See, Field, paragraph 0022. Thus, Field's "conduction cardiomyocytes" do not detect and monitor physiological activity *from a distance.* Instead, Field's conduction cardiomyocytes directly alter the contraction activity of the heart by "establishing depolarization waves in the heart." Thus, the cells taught by Field are not for monitoring from a distal site. Instead they are for changing the heart function through direct contact and interaction with heart tissues. As such, Field's cells have properties that are different from those of the in vitro or ex vivo modified stem cells of the present invention. For example, according to Field, while working cardiomyocytes express connexin43, Field expressly discloses that the conduction cardiomyocytes necessarily do not express connexin43 (see, Field at paragraph 0028, disclosing ways to kill cells that are not conduction cardiomyocytes).

Thus, there are factual and technical grounds establishing that the inherent feature (e.g., monitoring chronotropic activity at a site distant from the heart) *DOES NOT* necessarily flow as a necessary conclusion from the teaching of the cited art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Int. 1990); *In re Oelrich*, 666 F.2d 578, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981). Applicant therefore submits that Field does not expressly or inherently disclose every element of the present invention.

With regard to claim 75, the Examiner asserts that cardiomyocytes are capable of producing VEGF, but provides no evidence to support this allegation. Field makes no mention whatsoever of VEGF. Applicant submits that if the Examiner wishes to reject claim 75 over Field, such a rejection must be made using another reference that actually does at least mention cardiomyocyte production of VEGF. Absent such a showing, the Examiner has not made a proper rejection under section 102.

Applicant submits that Field fails to explicitly and/or inherently disclose every element of the claimed invention and respectfully requests withdrawal of this rejection of claims 74-76 and 80-84 under 35 U.S.C. § 102(e).

RESERVATION OF RIGHTS

In the interest of clarity and brevity, Applicant may not have addressed every assertion made in the Office Action. Applicant's silence regarding any such assertion does not constitute any admission or acquiescence. Applicant reserves all rights not exercised in connection with this response, such as the right to challenge or rebut any tacit or explicit characterization of any reference or of any of the present claims, the right to challenge or rebut any asserted factual or legal basis of any of the rejections, the right to swear behind any cited reference such as provided under 37 C.F.R. § 1.131 or otherwise, or the right to assert co-ownership of any cited reference. Applicant does not admit that any of the cited references or any other references of record are relevant to the present claims, or that they constitute prior art. To the extent that any rejection or assertion is based upon the Examiner's personal knowledge, rather than any objective evidence of record as manifested by a cited prior art reference, Applicant timely objects to such reliance on Official Notice, and reserves all rights to request that the Examiner provide a reference or affidavit in support of such assertion, as required by MPEP § 2144.03. Applicant reserves all rights to pursue any cancelled claims in a subsequent patent application claiming the benefit of priority of the present patent application, and to request rejoinder of any withdrawn claim, as required by MPEP § 821.04.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 30th day of August 2007.

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